

REMARKS / ARGUMENTS

Claims 1 through 6 and 8 through 18 are pending in the application

Claim Objections

The Examiner has objected to claims 16 and 17 because of formalities, namely that the claim identifiers were incorrect. Applicants have corrected the claim identifiers herewith.

Rejections Under 35 USC §102

The Examiner has rejected claims 1 through 4, 6, 16, and 17 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,340,744, issued to Leif et al.

Applicants note that claim 1 has been amended herewith. Claims 1 through 4, 6, 16, and 17 depend, either directly or indirectly, from claim 1. The present amendment to claim 1 requires that the luminescent resonance energy transfer solution does not comprise a micellar solution.

Support for this limitation is found throughout the specification of the application as filed. For example, page 25, lines 22-23, state: "In the unitary luminescence enhancing solution, the concentration of surfactant, when present, is less than the critical micellar concentration. In other words, a surfactant needed to produce micelles is either not present or is not present in sufficient concentration to result in micelle formation. Further, the Declaration of Dr. Robert C. Leif, already of record and dated March 28, 2009, notes that the present invention resulted from the unexpected discovery that a micelle-producing amount of at least one surfactant is not required for solid state luminescence.

The '744 patent is directed to a micellar solution. The aforementioned Declaration of Dr. Robert C. Leif underscores this point, as well as the shortcomings of such micellar solutions, and Applicants incorporate the Declaration here by reference. The Examiner has previously indicated the sufficiency of the Declaration.

Applicant submits that, as amended, claim 1 is patentable over the '744 reference.

Claims 2 through 4, 6, 16, and 17 depend, directly or indirectly, from claim 1 and are therefore allowable dependent claims depending from a patentable base claim.

The Examiner also rejects claims 1 through 4, 6, 16, and 17 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,750,005, issued to Leif et al.

Applicants note that the '005 patent suffers from the same deficiency as the '744 patent, discussed above, namely that the '005 patent is directed to a composition comprising a micellar solution. In the Summary of the Invention, column 2, line 9, the disclosure states: "In accordance with this invention, there is provided a spectrofluorimetrically detectable luminescent composition comprising water, *a micelle-producing amount of at least one surfactant*..." (emphasis added). Example I, column 16, of the patent is entitled "Enhancement of the EuMac Luminescence by Gd(III) in Aqueous Micellar Solutions Containing Appropriate Additives." Use of micellar solutions occurs throughout the '005 reference.

It should be noted that while the '005 patent does disclose solid-state luminescence, those solid-state compositions used also comprise micellar solutions. Example IV, column 21, is directed to "Solid-State Studies of the Luminescence Intensity of EuMac in Gd-Containing Optimized Cofluorescence Solutions." The Example notes that a strip of electrophoresis film was spotted with a co-fluorescence-optimized aqueous micellar solution. Further, the disclosure in this example states that the results of the experiment show "...that the cofluorescence effect for the EuMac, *once established in micellar solution*, is maintained in solid samples." (emphasis added).

Thus, even the solid composition of the '005 patent comprises a micellar solution, and claim 1 of the present application, as currently amended, is patentably distinct over that reference. It should be noted that it is known in the art that even the dry form of a micellar solution retains characteristics of the micellar composition. Applicants attach two references hereto in support of this. The first is entitled "Crust Effect on Multiscale Pattern Formations in

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Drying Micelle Solution Drops on Solid Substrates," *Langmuir* 2004, 20, 9520-9525. This reference is attached in its entirety. Also attached is an abstract from the journal *Polymer*, relating to an article entitled "Micropatterning from drying micelle solution of diblock copolymers: strap-structure, quadrate farmland-structure and biometric structure." These references are not held out to be directly related to the present application, but are provided to demonstrate that dried micellar solutions retain characteristics pertinent to micellar character of the solution. The *Langmuir* reference, for example, states on page 9521: "In our study, we examined the pattern formation in the drying of relatively concentrated solution drops containing spherical micelles on solid substrates." The *Polymer* reference states in the Abstract thereof: "Micropatterns of strap and farmland structures...were obtained by drying the micelle solutions....It is believed that solvent evaporation and micelle migration account for the observed micelle micropatterns." Again, these references are not held out as being pertinent to the present invention except in that they establish that it is known that drying micellar solutions results in a dry formation that retains characteristics derived from the micellar character of the solution. Applicants submit that the dry compositions disclosed in the '005 reference comprise micellar solutions and therefore fall outside of the scope of claim 1 of the present application, as amended. Further, because the use of micellar solutions is essential to the functionality of the compositions of the '005 patent, that reference teaches away from the present invention, which is based on the unexpected discovery that the present compositions provide solid-state luminescence without comprising a micelle-producing amount of at least one surfactant.

In view of the above, Applicants submit that claim 1 of the present application is patentable over the '005 reference. Claims 2 through 4, 6, 16, and 17 depend, directly or indirectly, from claim 1 and are therefore allowable dependent claims depending from a patentable base claim.

Applicants note that the Examiner invites the Applicants to overcome the §102(e) reference by submission of a Declaration under 1.132 that any invention disclosed but not claimed in the '005 reference was derived from the inventor of the present application. For the

reasons stated above, Applicants believe the '005 reference has been overcome and that such a showing is not necessary. Applicants therefore remain silent on the matter, but reserve the right to make such a showing, if the facts support it, at a future time.

The Examiner rejects claims 1 through 6 and 16 through 18 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,340,744, issued to Leif et al., in view of U.S. Patent No. 4,927,923, issued to Mathis et al.

Applicants note that claim 1 has been amended herewith to require that the composition does not comprise a micellar solution. As such, claim 1 is allowable over the '744 reference for the reasons stated above. The arguments above are incorporated here with respect to this rejection, by reference. Claims 2 through 6 and 16 and 17 are dependent, either directly or indirectly, on claim 1, and are therefore also allowable for the reasons stated above.

Applicants have also amended claim 18 herewith to require that the composition does not comprise a micellar solution. Thus, claim 18 is allowable over the '744 reference for the same reasons as claim 1, and the same arguments used with respect to claim 1 are incorporated here by reference with respect to claim 18.

In view of the foregoing, Applicants submit that claims 1 through 6 and 16 through 18 are allowable over the combination of Leif et al. ('744) and Mathis et al.

The Examiner also rejects claims 1 through 6 and 16 through 18 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,750,005 issued to Leif et al., in view of U.S. Patent No. 4,927,923, issued to Mathis et al.

Applicants note that claim 1 has been amended herewith to require that the composition does not comprise a micellar solution. As such, claim 1 is allowable over the '005 reference for the reasons stated above. The arguments above are incorporated here with respect to this rejection, by reference. Claims 2 through 6 and 16 and 17 are dependent, either directly or indirectly, on claim 1, and are therefore also allowable for the reasons stated above.

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Applicants have also amended claim 18 herewith to require that the composition does not comprise a micellar solution. Thus, claim 18 is allowable over the '005 reference for the same reasons as claim 1, and the same arguments used with respect to claim 1 are incorporated here by reference with respect to claim 18.

In view of the foregoing, Applicants submit that claims 1 through 6 and 16 through 18 are allowable over the combination of Leif et al. ('005) and Mathis et al.

The Examiner rejects claims 8, 9, and 11 through 13 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,316,909, issued to Xu, in view of U.S. Patent No. 6,750,005, issue to Leif et al.

Applicants note that claim 8 has been amended herewith to include the limitation that the luminescence enhancing solution does not comprise a micellar solution. The Examiner states that the cofluorescent complexes of Xu are single-phase as they do not necessarily require a detergent (surfactant) to generate micelles for solid state luminescence. The Examiner cites column 4, lines 1 through 32, of Xu. Applicants disagree with this reading of Xu.

The presence of a detergent is required in all of the embodiments of the disclosed Xu invention. In column 4, line 22, Xu states: "In most of the cofluorescence complexes the presence of a detergent, such as TRITON X-100, TRITON X-100, TRITON N-101, and TRITON X-405 has an effect on the fluorescence intensity and its stability. The micelles formed protect the fluorescent chelates from the quenching action by the water and at the same time keep the cofluorescence complex in suspension." This statement *does not* say that detergents are not required for solid state fluorescent luminescence. Instead, the statement is that micelle-forming detergent is necessary in Xu, but not always sufficient. The statement means that some of the complexes were not affected by the detergents. Those complexes were not protected from the quenching action of water. In other words, these complexes of Xu did not work. It should be noted that each and every Example used by Xu, Examples which, in the words of Xu, illustrate the invention, requires the use of a detergent. Example 1 requires TRITON X-100

surfactant. Example 2 requires TRITON X-100. Example 3 required TRITON X-100. Example 4 requires TRITON X-100. Example 5 is based on the Ea and Eb solutions of Example 1 and as such requires TRITON X-100. Example 6 requires the Ea and Eb solutions of Example 2 and as such requires TRITON X-100. Again, the detergent of Xu was effective in most of the cofluorescence complexes of Xu, but was ineffective in others. Xu does not state that detergent is needed in only *some* of the compositions for effective luminescence. As noted above, the present invention is a significant and unexpected advance in the art.

It should also be noted that the invention of Xu is non-analogous art as compared to the present invention. The invention of Xu includes a dissociation step that results in the lanthanide labeling ion being removed from its original complex and being transferred to another complex. This step does not occur in the present invention. The purpose of the macrocycle of the present invention is to strongly bind the lanthanide so that it will not exchange with other lanthanides or move from its binding location. In order to function in cytometry (quantitative measurements on individual cells), a label must remain bound to its analyte. Thus the chemistry of Xu and the present invention are quite different in this important respect.

In view of the foregoing, Applicants submit that claim 8 is allowable over the cited art. Further, claims 9 and 11 through 13 depend, directly or indirectly, from claim 8 and are therefore allowable dependent claims stemming from a patentable base claim.

The Examiner rejects claims 14 and 15 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,696,240, issued to Vallarino et al., in view of U.S. Patent No. 5,316,909, issued to Xu, and further in view of U.S. Patent No. 6,750,005, issued to Leif et al.

The Examiner notes that the Vallarino et al. '240 reference does not disclose the luminescence enhancing solution of the instant claims. The Examiner relies on Xu '909 and Leif et al. '005 to remedy this deficiency in Vallarino et al. Applicants note, however, that claims 14 and 15 of the present application have been amended herewith. As amended, both claims require that the luminescence enhancing solution be a single-phase, non-micellar solution. This

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limitation renders the claims patentable over both Xu and Leif et al. '005 for the reasons stated with respect to those references, above. Those same arguments are incorporated here by reference. Applicants submit that claims 14 and 15 are therefore allowable over the combination of references cited by the Examiner.

Other Claim Amendments

Claims 16 and 17 have been amended herewith to remove the negative limitations in the claim and recite the use of an ionic compound of gadolinium (III) and a complex of gadolinium (III), respectively. Applicant submits that given the current amendments to the claims, these two dependent claims are now allowable dependent claims stemming from patentable base claims.

Allowable Subject Matter

The Examiner has objected to claim 10 as being dependent upon a rejected base claim, but indicates that claim 10 would be allowable if rewritten in independent form. Applicants thank the Examiner for so noting. Applicants submit, however, that claim 10 is now in condition for allowance as depending from claim 8, which is allowable for the reasons stated above.

Applicant submits that, in view of the foregoing, all pending claims in the present application, namely claims 1 through 6 and 8 through 18, are allowable over the cited art. Applicant kindly requests a Notice of Allowance in this case.

No new matter has been added with this Amendment and Response.

If any action can be taken on the part of Applicants to expedite the Allowance of this application, the Examiner is invited to contact the undersigned via telephone or email.

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Respectfully Submitted;



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